

# Cell-cell communication in the malaria parasite

By Anna Rivkin

MeBop 2017

Bern, Switzerland

# Where?

- Israel



# Where?

- Israel
- **Weizmann institute of science**  
Established in 1934 by Chaim Weizmann



# Where?

- Israel
- Weizmann institute of science
- The laboratory of Dr. Neta Regev Rudzki



# What?

- We study **cell-cell communication** in the **malaria parasite**

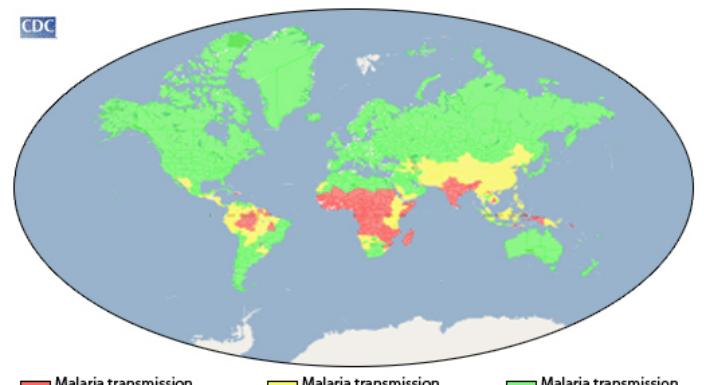
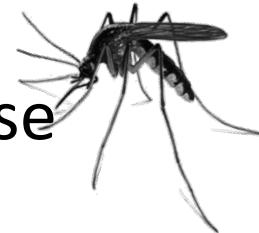
# Malaria Disease

- One of the most severe health problems worldwide
- Affects 3.2 billion people each year
- A leading cause of death and disease - 438,000 deaths annually
- Most affected groups: young children and pregnant women



# Malaria Disease

- A mosquito-borne disease
- Caused by the protozoan **parasite** of the genus ***Plasmodium***
- Occurs mostly in tropical and subtropical areas of the world



Malaria transmission occurs throughout

Malaria transmission occurs in some parts

Malaria transmission is not known to occur

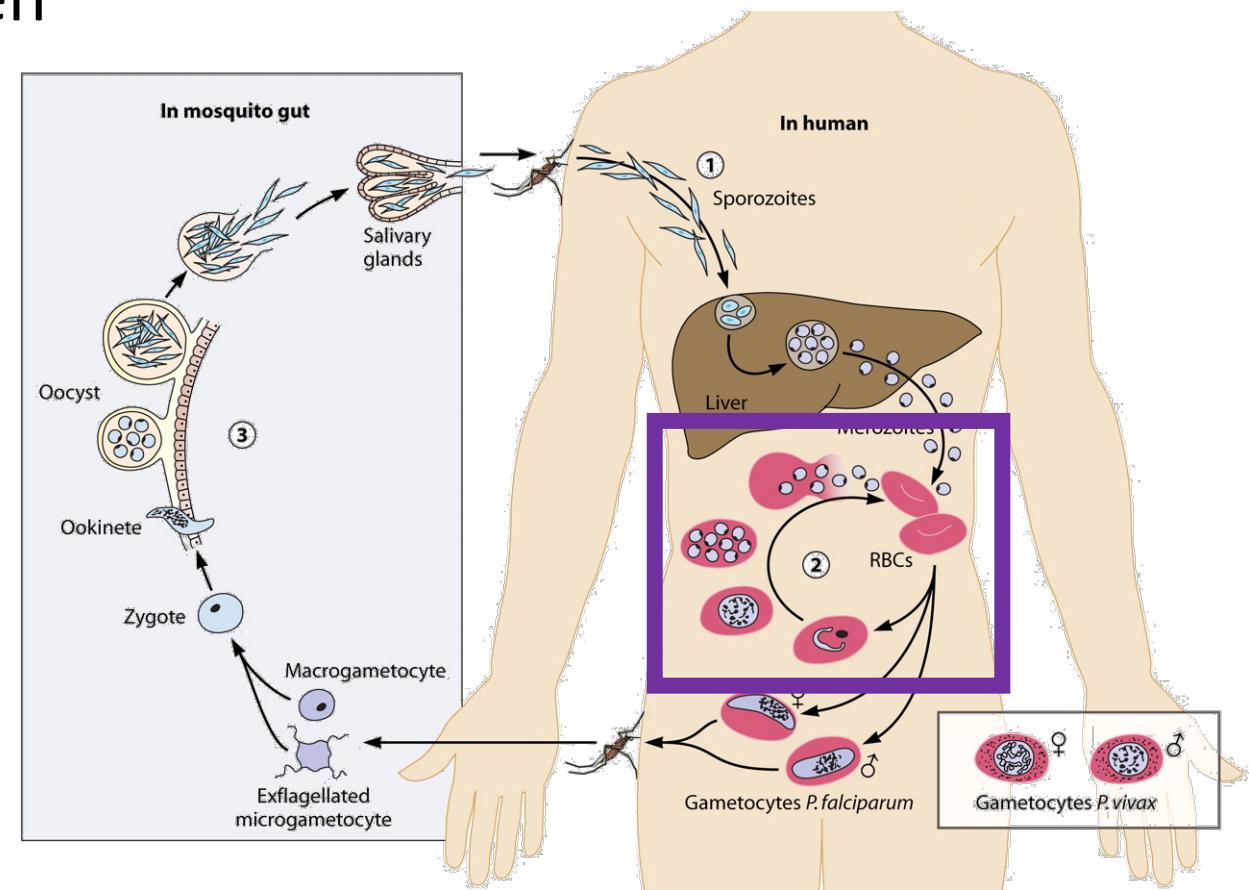
# Malaria Disease

- No effective vaccine available
- Increasing levels of resistant strains- new drugs needed

**Basic research is essential to understand the biology of the parasite**

# *Plasmodium falciparum* (*Pf*)

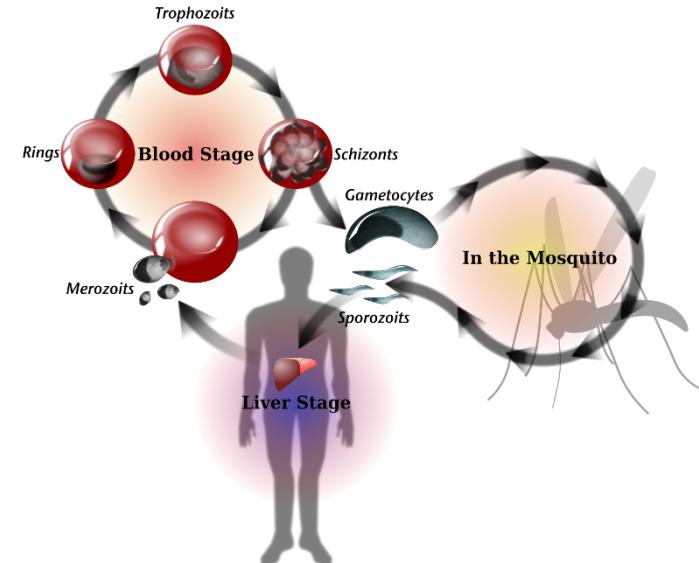
- Complex life cycle - shifts between the mosquito vector and the human host
- We grow the parasites in human red blood cells



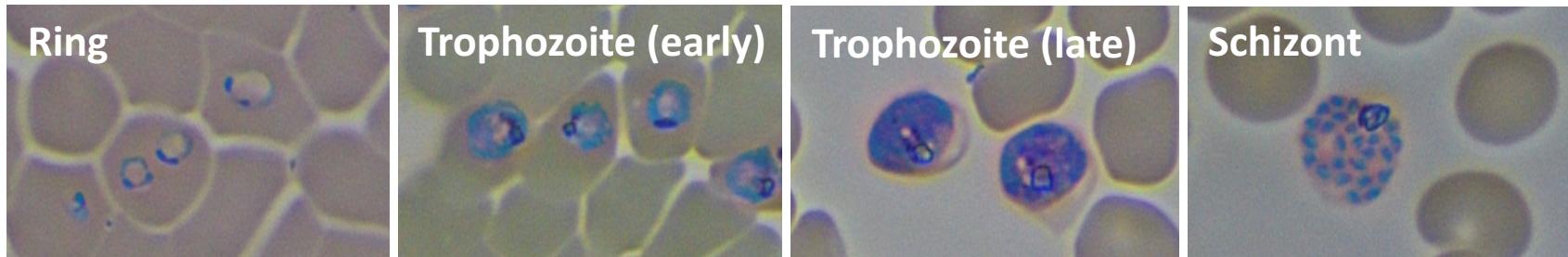
Bousema & Drakeley, Clin. Microbiol, 2011

# *Pf* blood stage in-vitro system

- Intracellular parasite
- Grow *Plasmodium falciparum* in human red blood cells (RBCs).
- Feed them with RPMI media and human RBCs
- Grown in special boxes with specific gas mix



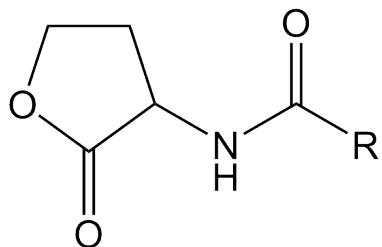
# *Plasmodium falciparum* blood stage



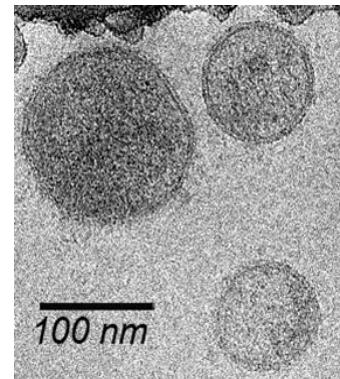
# Cell-cell communication

- Cell-cell communication and social behavior is established in many eukaryotes and prokaryotes via various mechanisms.

Small molecules

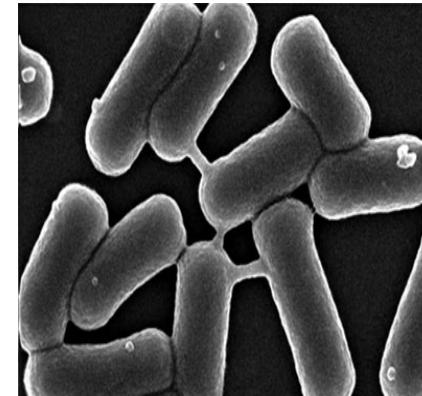


Extracellular vesicles



Electron Microscopy platform, CIC bioGUNE

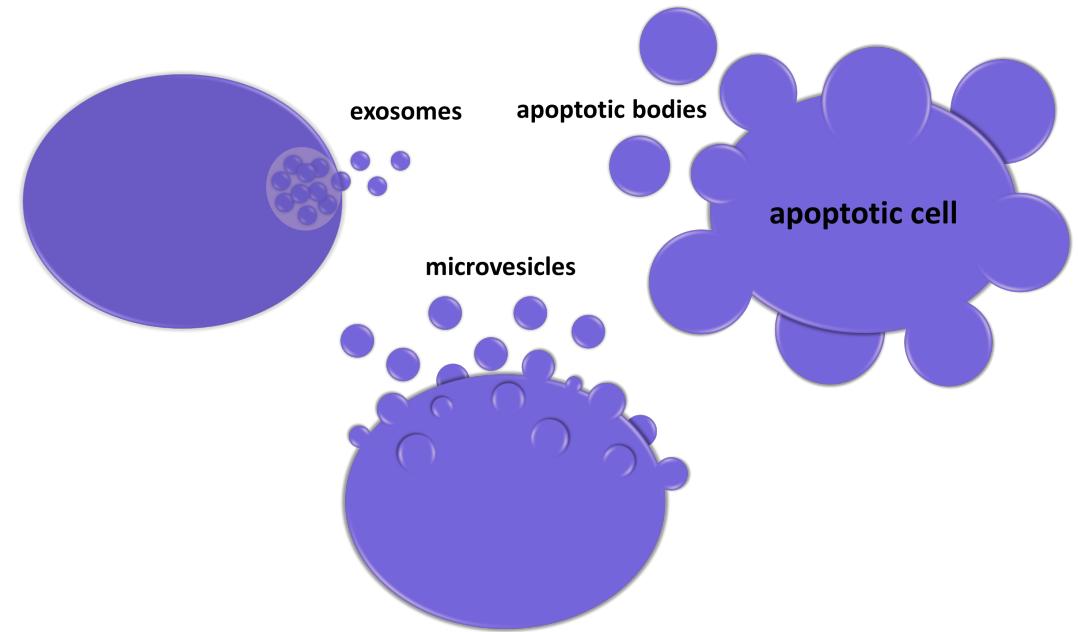
Nanotubes



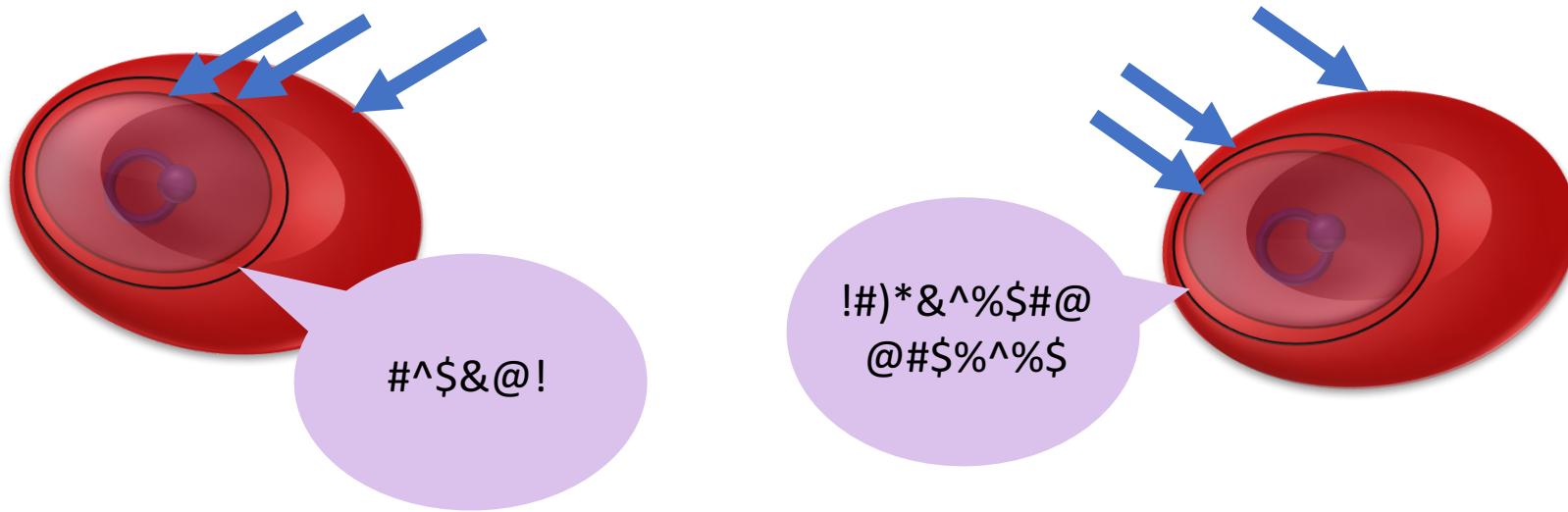
Dubey and Ben-Yehuda, 2011

# Extracellular vesicles

- Membrane-contained, nanometer-sized, vesicles released by cells
- Classified into 3 main groups:
  - a) Microvesicles
  - b) Exosomes
  - c) Apoptotic bodies



# Cell-Cell Communication in Malaria?



It was recently established *Pf*RBCs communicate with one another via **exosome-like vesicles**.

# Cell-Cell Communication in Malaria!!!

The image shows a journal cover from the journal 'Cell' (Resource). The title of the paper is 'Cell-Cell Communication between Malaria-Infected Red Blood Cells via Exosome-like Vesicles'. The authors listed are Neta Regev-Rudzki, Danny W. Wilson, Teresa G. Carvalho, Xavier Sisquella, Bradley M. Coleman, Melanie Rug, Dejan Bursac, Fiona Angrisano, Michelle Gee, Andrew F. Hill, Jake Baum, and Alan F. Cowman. The cover includes several institutional affiliations and correspondence information.

**Cell**

**Resource**

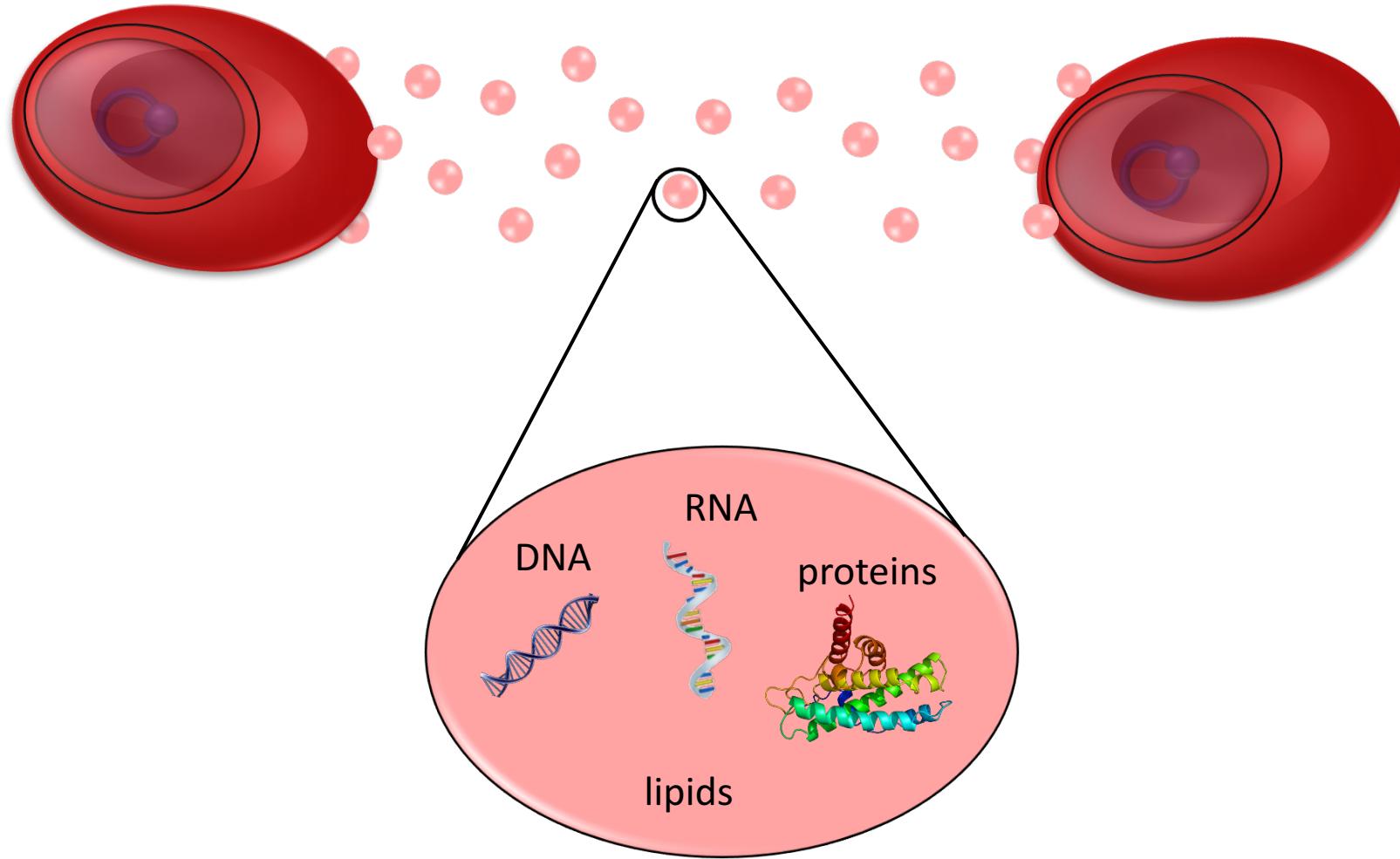
**Cell-Cell Communication between Malaria-Infected Red Blood Cells via Exosome-like Vesicles**

Neta Regev-Rudzki,<sup>1,2,6</sup> Danny W. Wilson,<sup>1,2,6</sup> Teresa G. Carvalho,<sup>1,2,7</sup> Xavier Sisquella,<sup>1,2</sup> Bradley M. Coleman,<sup>3,4</sup> Melanie Rug,<sup>1,2,8</sup> Dejan Bursac,<sup>1,2</sup> Fiona Angrisano,<sup>1,2</sup> Michelle Gee,<sup>5</sup> Andrew F. Hill,<sup>3,4</sup> Jake Baum,<sup>1,2</sup> and Alan F. Cowman<sup>1,2,\*</sup>

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<sup>\*</sup>Correspondence: cowman@wehi.edu.au  
<http://dx.doi.org/10.1016/j.cell.2013.04.029>

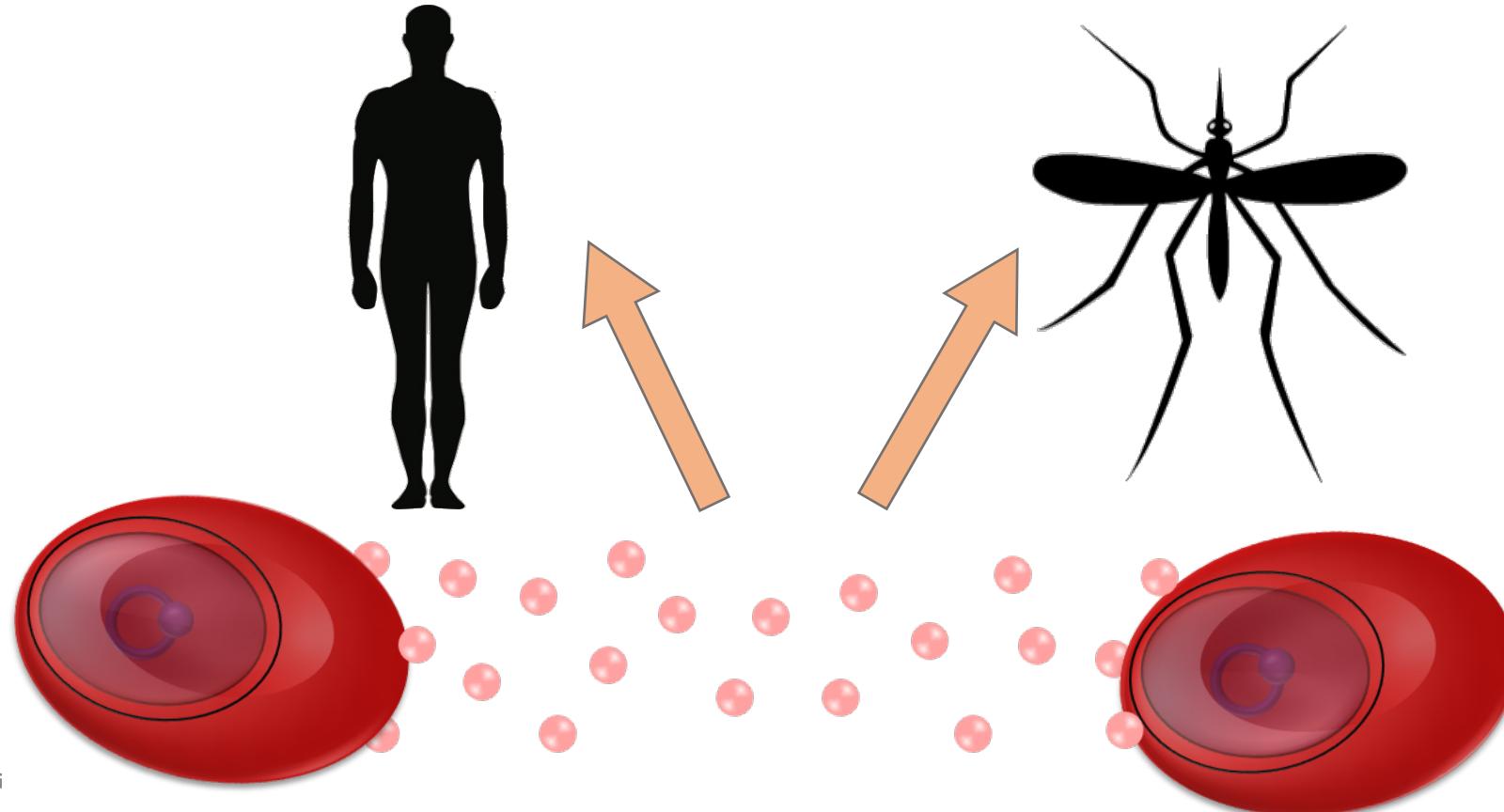
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# Cell-Cell Communication in Malaria



# Main research questions

- How do infected RBC derived vesicles affect the host cells?



# Main research questions

- How do infected RBC derived vesicles affect the host cells?
- Phospho-proteomics analysis of host THP1 cells (monocyte cell line) revealed unique phosphorylation patterns
- Study MAPK pathway in this context.

# Unique skills and expertise

- Plasmodium culturing
  - ✓ Routine cultures
  - ✓ Growth assays
- Biochemistry and molecular assays
  - ✓ RNA, DNA, Protein work
- **Isolation and characterization of extracellular vesicles**
  - ✓ Optiprep / ultracentrifugation
  - ✓ AFM, TEM, nanosight
  - ✓ Vesicle staining
  - ✓ Uptake assays
  - ✓ Vesicle cargo analysis

# Difficulties in our local area

- Malaria was eradicated from Israel in 1962- No mosquito model available
- Only few samples from affected individuals are available

Questions?

# Invitation!

THE BATSHAVA DE ROTHSCHILD SEMINAR ON  
**FRONTIERS IN PARASITOLOGY**

**March 5-8, 2018**

The David Lopatie Conference Centre,  
Weizmann Institute of Science



**Travel fellowship for students that will fully cover the travel and accommodation of African students are available**

Merci!

Asante!

Thank you!

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Asante!

Merci!